CLAIMS

1. A method for prenatal diagnosis of foetal cells isolated from maternal blood, comprising the following steps:

a) filtering a sample of pure or diluted maternal blood to concentrate on a filter according to size, certain circulating cells, and in particular cells of foetal origin;

b) analyzing the cells retained on the filter to obtain a presumption or identification of their foetal or maternal origin;

c) demonstrating the foetal origin of certain enriched cells by genetic analysis of individually isolated cells;

d) identifying genetic anomalies specifically targeted to individually analyze cellular genomes for which a foetal origin has been demonstrated.

2. A method according to claim 1, characterized in that the foetal or maternal origin of the cells in step c) is identified by seeking genetic marker(s) characteristic of foetal cells.

3. A method according to claim 1 or claim 2, characterized in that the cells retained on the filter are collected individually.

4. A method according to claim 3, characterized in that the cells retained on the filter are collected individually by microdissection.

5. A method according to claim 4, characterized in that microdissection consists of laser cutting the portion of the filtration membrane on which a cell is retained or detaching the cell using a laser then recovering the single collected cell in a suitable tube.

6. A method according to claim 5, characterized in that step d) is carried out on the genome of a single collected cell.

7. A method according to claim 6, characterized in that genetic analysis of the genome of a single collected cell (i) demonstrates the foetal or maternal origin of said cell and (ii) allows identification of genetic or chromosomal anomalies of the foetus or of a particular genotype thereof if the foetal origin of said cell is demonstrated.

8. A method according to claim 7, characterized in that the foetal or maternal origin of a collected cell is demonstrated by identification on a DNA preparation derived from the genome of the single collected cell of one or more genetic markers or of polymorphism, of a combination of said markers or of a particular allele assay of said markers, demonstrating the biparental contribution of the foetal DNA.

9. A method according to claim 7 or claim 8, characterized in that a genetic or chromosomal anomaly of the foetus or of a particular genotype thereof is carried out by identifying a genetic target on a preparation of DNA derived from the genome of the single collected cell.

10. A method according to any one of claims 7 to 9, characterized in that prior to demonstrating the foetal or maternal origin of a single collected cell and/or identifying a genetic or chromosomal anomaly of the foetus or of a particular genotype thereof, said collected cell is lysed and its entire genome is preamplified and purified to obtain a preparation of preamplified DNA derived from the genome of a single collected cell.

11. A method according to claim 10, characterized in that the foetal or maternal origin of a collected cell is demonstrated then a genetic or chromosomal anomaly of the foetus or of a particular genotype thereof is identified by amplification of genetic markers or of polymorphism or of a combination of said markers or one or more sequence(s) carrying the

identified genetic target(s), from the preamplified DNA preparation derived from the genome of said cell.

12. A method according to claim 11, characterized in that amplification of at least one genetic marker or of polymorphism or of at least one sequence carrying a genetic target is carried out from less than one fifth of the preamplified DNA preparation.

13. A method according to claim 11 or claim 12, characterized in that the foetal or maternal origin of a collected cell and/or identification of a genetic or chromosomal anomaly of a foetus or of a particular genotype thereof is demonstrated by sequencing amplified genetic targets or markers.

14. A method according to claim 10, characterized in that the foetal or maternal origin of a collected cell is demonstrated and/or a genetic or chromosomal anomaly of the foetus or of a particular genotype thereof is identified by hybridization of all or a portion of the preamplified DNA preparation with specific DNA probes or PNA (Peptide Nucleic Acid) type probes.

15. A method according to claim 14, characterized in that the specific DNA probes are fixed on a support forming a DNA micro- or macro-array.

16. A method according to any one of claims 9 to 15, characterized in that at least one polymorphism marker to be identified is a microsatellite marker, a VNTR (Variable Number of Tandem Repeats) marker, a SNP (Single Nucleotide Polymorphism) marker or a STR (Short Tandem Repeat) marker.

17. A method according to any one of claims 9 to 16, characterized in that the foetal or maternal origin of a collected cell is demonstrated by identifying a marker or a combination of markers or on allele assay of said markers distinguished from those detected on the genome of non maternal cells, in particular by seeking the genome of said collected cell, a marker or a combination of markers specific to the DNA of paternal cells.

18. A method according to claim 10, characterized in that a chromosomal anomaly is identified by a method for comparative genomic hybridization (CGH) of a preamplified DNA preparation derived from the genome of a single collected cell and the foetal origin of which has been demonstrated, and of a preamplified DNA preparation of cells or maternal origin or non foetal reference cells.

19. A method according to claim 1, characterized in that prenatal diagnosis of a chromosomal anomaly or the sex of a foetus is carried out by in situ hybridization of a specific probe for a chromosomal anomaly of the gender to be detected on the genome of cells retained on the filter.

20. A method according to any one of claims 1 to 19, characterized in that the filtered maternal blood is derived from a blood sample made after the fifth week of pregnancy.

21. A method according to any one of claims 1 to 20, characterized in that the genetic analysis of cells retained on the filter is carried out by filtering 1 to 10 ml of maternal blood.

22. A method according to any one of claims 1 to 21, characterized in that the maternal blood sample is diluted 10 to 100 fold in a filtration solution.

23. A method according to any one of the preceding claims, characterized in that the pure or diluted maternal blood sample is filtered using a filter with a pore size in the range 6 to 15 μm, preferably pores with a diameter of about 8 μm.

24. A method according to claim 23, characterized in that the filter has pores with a diameter of about 8 μm and a pore density in the range 5×10^4 to 5×10^5 pores/m^2.

25. A method according to any one of claims 1 to 24, characterized in that the filter is a polycarbonate filtration membrane the pore size of which is graded.

26. A use of a filtration device for obtaining foetal cells present in maternal blood and comprising, on a frame:

- a porous filter that can retain certain circulating cells according to their size, mounted between two clamping devices, respectively upstream and downstream with respect to the filtration direction, and providing a filtration seal;
- the upstream block comprising means for storing and/or pre-treating the samples to be analyzed;
- the downstream block comprising perforations facing the storage means;
- means for forced filtration.

27. Use according to claim 26 of an ISET type filtration device in which the applied filtration pressure is in the range 0.05 bars to 0.8 bars, preferably 0.1 bars.

28. Use according to claim 26 or claim 27 of a ISET type filtration device for isolating foetal cells from maternal blood and comprising a filter with a mean pore size in the range 6 μm to 15 μm, preferably about 8 μm.

29. Use according to claim 28 of a ISET type device in which the filter has pores with a diameter of about 8 μm and a pore density in the range 5×10^4 to 5×10^5.